REMARKS

I. Status of the Claims.

Claims 1, 5-12, 18, 25, 29, 32-34 and 38 are pending in the Application. The Examiner has acknowledged that Claim 38 contains allowable subject matter. This Response and Amendment amends Claims 1 and 12; and adds new claims 39-42.

II. Claim Amendments and New Claims.

Applicants respectfully request entry and consideration of the claim amendments and new claims described below.

A. Claims 1 and 12.

Claims 1 and 12 are amended to remove the term "macromolecule." In addition, Claim 12 is amended to correct the spelling of the word "use." Accordingly, the amendments to the claims do not add new matter.

B. Claim 39

New claim 39 is added to provide a dependent claim for a preferred version of the invention, "wherein the biological molecule is a drug of abuse or metabolite thereof." Support for the new claim can be found throughout the specification, for example, see page 4, lines 26-31. Accordingly, this new claim does not add new matter.

C. Claim 40

New claim 40 is added to provide a dependent claim for another preferred version of the invention, "wherein the drug of abuse is selected from the group consisting of cocaine, morphine, and nicotine." Support for the new claim can be found throughout the specification, for example, see page 4 lines 29-31. Accordingly, this new claim does not add new matter.

D. Claim 41

New claim 41 is added to provide a dependent claim for another preferred version of the invention, "wherein the biological molecule is a therapeutic drug selected from the group consisting of tobramycin, phenobarbitol, theophylline, digoxin, tobramycin, phenobarbitol, theophylline, digoxin, and gentamycin." Support for the new claim can be

found throughout the specification, for example, see page 4, line 31 to page 5 line 1. Accordingly, this new claim does not add new matter.

E. Claim 42

New claim 42 is added to provide an independent claim for another version of the invention, wherein the solid support is "formed from a material selected from the group consisting of cellulose, agarose, polypropylene, polymethacrylate, and nylon," "the activating compound is 1,2,4-carbonyl di-triazole," and "the biological molecule is selected from the group consisting of hormones, therapeutic drugs, and drugs of abuse." Support for the new claim can be found throughout the specification, for example, see page 6 lines 9-13, page 7 lines 9-13, and page 4 lines 26-29. Accordingly, this new claim does not add new matter.

III. Objections to the Claims

Claim 12 is amended to replace the word "used" with "use" as suggested by the Examiner.

IV. 35 USC § 112 Rejection

Claims 1, 5-12, 18, 25 and 32-34 are rejected under 35 USC 112, first paragraph for containing new matter. Claims 1 and 12 are amended to remove the term "macromolecule" to obviate the rejection.

V. 35 USC § 103 Rejection.

Claim 29 is rejected under 35 U.S.C. § 103(a) as unpatentable over Swenson et al. in view of Stolowitz et al. and Gasson as evidenced by Tripathi et al. and Gehlson for the reasons stated in numbered paragraph 6 of the Office Action. Applicants respectfully traverse this rejection because the Office has not established a *prima facie* case of obviousness. Applicants respectfully request withdrawal of the rejection and allowance of pending claim 29 on the following basis.

A. Swenson et al. does not disclose step (b) of the claimed method.

Swenson et al. teaches a method of synthesizing luteinising-hormone releasing hormone (LHRH) antagonists having various substitutions at the N-epsilon amine of

DLys at position 6 of the synthetic peptide. One of these substitutions is DLys(Histaminecarbonyl). The modified peptide is subsequently cleaved from the MBHA resin serving as a solid support during solid phase peptide synthesis (SPPS).

The Office cites Tripathi et al. to show that the MBHA resin of Swenson et al. provides a polystyrene support having at least one available amino group, specifically, 4-methyl benzhydrylamine. Applicants respectfully disagree with the Office's characterization of Swenson et al. (page 653, paragraph 2) as disclosing "(b) reacting the available amino group on the solid support with an activating compound." Swenson et al. treat the peptide-resin with 1,1'-carbonyldiimide. Since the MBHA resin is linked to the peptide via an amide bond during SPPS, the amino group on the MBHA resin is no longer available for activation.

B. Swenson et al. does not fairly suggest providing a hormone or therapeutic drug consisting of histamine

The Office Action pinpoints the histamine side group attached to the decapeptide in Swenson et al. as providing a biological molecule qualifying as a hormone and/or therapeutic drug.

> "[I]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill of the art." *In re Wesslau* 353 F.2d at 241, 225 USPQ at 393 (CCPA, 1965).

Applicants respectfully submit that, to one of ordinary skill in the art, the hormone(s) and/or therapeutic drug(s) attached to a solid support suggested by Swenson et al. would be the substituted Luteinising-hormone releasing hormone (LHRH) antagonists as a whole, not merely the histamine side group attached to one of the amino acids. Indeed, histamine release is considered an undesirable side effect associated with the use of LHRH antagonists and is not inherently "therapeutic" in this context. See, e.g., US4935491: Effective antagonists of the luteinizing hormone releasing hormone which release negligible histamine.

3. Swenson et al. does not disclose step (d) of the claimed method.

Applicants further disagree with the Office's characterization of Swenson et al.

(page 653, paragraph 2) as disclosing "(d) reacting the biological molecule with the activated support thereby covalently attaching the biological molecule to the solid support so that the biological molecule is available for use in an assay." As described above, treatment of the peptide-resin with 1,1'-carbonyldiimide does not form an activated resin. Moreover, subsequent treatment with the "appropriate amine" covalently attaches substituents to the peptide, not the solid support.

4. Swenson et al. does not disclose 1,2,4-carbonyl di-triazole and neither Stolowitz et al. nor Gasson teach the equivalence of carbonyldiimide and 1,2,4-carbonyl di-triazole as coupling reagents

The Office admits Swenson et al. fails to teach an activating compound such as 1,2,4-carbonyl di-triazole and cites Stolowitz et al. and Gasson as disclosing equivalent coupling compounds to the 1,1'-carbonyldiimide used by Swenson et al.

As a preliminary matter, Applicants respectfully disagree with the characterization of Gasson as teaching the substitution of 1,2,4-carbonyl di-triazole as an art recognized coupling agent. Once again, the Office has taken the last paragraph on page 20 of Gasson completely out of context. Gasson, page 20, last paragraph, merely lists a number of condensing agents, such as a carbodiimide, a suitable carbonyl compound (like N,N'-carbonylditriazole) and an oxazolinium salt, which may be used to introduce an acyl group in cephalosporin compounds. Picking and choosing a specific compound used for an entirely different purpose in the cited reference indicates the impermissible use of hindsight to show obviousness.

Moreover, although the combined references of Stolowitz et al. and Gasson mention a variety of "azolides" or "condensing agents," including N, N'-carbonyl-diimidazole, N,N'-carbonyldipyrazole, N,N'-carbonyldi-1,2,3-triazole, N,N'-carbonyldi-1,2,4-triazole, N,N'-carbonydiindole, N,N'-carbonylidibenzimidazole, N,N'-diethyl-, dipropyl-, or diisopropyl-carbodiimide, N,N'-di-cyclohexyl-carbodiimide, and N-ethyl-N'-[3-(dimethylamino)propyl]carbodiimide, nowhere in this exhaustive laundry list of compounds is found the 1,1'-carbonyldiimide disclosed by Swenson et al. Accordingly, the Office's contention that "Stolowitz et al. and Gannon (*sic*) stand for the proposition that a carbonyldiimide and 1,2,4-carbonyl di-triazole represent 'equivalent' coupling reagents" lacks support in the cited references.

5. The proposed combination of Swenson et al. in view of Stolowitz et al. and Gasson does not produce the claimed invention

The Office Action states: "It would be prima facie obvious to one of ordinary skill in the art at the time of the invention was made to substitute the 1,2,4-carbonyl di-triazole coupling agent as disclosed by the combined teachings of Stolowitz et al. and Gasson to couple the compounds listed in Table 1 of Swenson et al. [to] the immobilized peptide because all of these reagents are art recognized coupling reagents." However, the combined teachings of Stolowitz et al and Gasson fail to cure the deficiencies of Swenson et al. As set forth above, the proposed combination would not be "(b) reacting the available amino group on the solid support with an activating compound," because the amino group on the MBHA resin of Swenson et al. would no longer be available for activation. Moreover, subsequent coupling of the compounds listed in Table 1 of Swenson et al. covalently attaches the substituents of Table 1 to the peptide, not the solid support. Accordingly, the combined references fail to teach or suggest all the claim limitations.

Further, in order to render the present claims obvious, there must be something in the prior art to suggest not only the desirability of combining the references, but a suggestion that they be combined in the particular manner and configuration as the claimed invention. *Uniroyal, Inc. v. Rudkin Wiley Corp.*837 F.2d 1044, 1051, 5 USPQ 2d 1434 (Fed. Cir. 1988), cert. denied, 488 U.S. 825 (1988). The Patent and Trademark Office has not identified any such suggestion.

In view of the foregoing, it is apparent that the Office Action's determination of obviousness is based on the hindsight combination of components selectively culled from the prior art in an attempt to fit the parameters of the claimed invention. *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534,546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). Applicants respectfully submit that the Office has not established the requisite *prima facie* case of obviousness with respect to Claim 29 and request withdrawal of the rejection on this basis.

CONCLUSION

The Applicants believe that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the

undersigned directly if there are any issues that can be resolved by telephone with the Applicants' representative.

If any extension of time is required for this response, such extension is hereby requested. The Commissioner is hereby authorized to charge payment of any fees associated with this communication, if such fees are due, to Deposit Account No. 19-2090.

Respectfully Submitted,

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